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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,960	05/09/2005	Bill Clark	PN0222	7113

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EXAMINER	
KILPATRICK, BRYAN T	
ART UNIT	PAPER NUMBER
4112	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,960	CLARK ET AL.	
	Examiner	Art Unit	
	BRYAN T. KILPATRICK	4112	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8 and 11-27* is/are pending in the application.

4a) Of the above claim(s) *11-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/19/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-10, in the reply filed on August 11, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 2, 3, 9, and 10 have been cancelled by Applicant.

3. Claims 11-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group II, there being no allowable generic or linking claim. Election was made in the reply filed on August 11, 2008.

Priority

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1, 4-8, and 24-27 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 10-16 of copending Application No. 2005/0232864 (CLARK et al.). Although the conflicting claims are not identical, they are not patentably distinct from each other because they claim similar material.

Specifically, instant claim 1 states a method of determining *in vivo* protein activity comprised of hyperpolarisng NMR active nuclei of samples collected from humans or non-humans preadministered with at least two probe compounds containing at least one NMR active nuclei, and analyzing the samples by NMR spectroscopy. Claims 1-3 of CLARK et al. states a method of phenotyping comprised of determining *in vivo* protein activity by hyperpolarising the NMR active nuclei of samples collected from a human preadministered with at least one probe compound were at least one probe compound contains at least one NMR active nuclei, and analyzing the samples by NMR spectroscopy. Instant claim 4 states the probe compounds are enriched with NMR active nuclei, claim 10 of CLARK et al. states that at least one probe compound is enriched with NMR active nuclei. Instant claim 5 states the hyperpolarising step is

carried out by one of means of polarization transfer from a noble gas, brute force, dynamic nuclear polarization (DNP), and spin refrigeration; claim 11 of CLARK et al. meets this same limitation. Instant claim 6 sates the collected samples are biofluids, claim 12 of CLARK et al. states the same limitation. Instant claim 7 states the probe compounds are substrates, inducers, or inhibitors for Cytochrome P450 (CYP450); this limitation is met by claim 14 of CLARK et al. Instant claim 8 states CYP1A2, CYP2A6, CYP2C8/9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4; this limitation is met by claim 15 of CLARK et al. Instant claim 24 and 26 state the probe compounds are enriched with at least one of ^{13}C and ^{15}N NMR active nuclei, claim 10 of CLARK et al states that at least one probe compound is enriched with NMR active nuclei. Instant claims 25 and 27 state a list of proteins and probe compounds used for determining protein activity; claims 13 and 16 of CLARK et al. state the same proteins and compounds for determining protein activity, respectively. Therefore the claimed invention would have been obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 5-6, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by W.O. 97/37239 A1 (PINES et al.).

Instant claim 1 states a method of determining *in vivo* protein activity comprised of hyperpolarisng NMR (nuclear magnetic resonance) active nuclei of samples collected from humans or non-humans preadministered with at least two probe compounds containing at least one NMR active nuclei, hyperpolarisng NMR active nuclei of samples collected from humans or non-humans with at least two probe compounds and at least one putative drug, and then analyzing and comparing the samples by NMR spectroscopy to identify protein activity caused by the putative drug. PINES et al. discloses on pages 4-5 the analysis of samples using hyperpolarized noble gas with NMR or MRI (magnetic resonance imaging), and the third paragraph of page 10 discloses hyperpolarized gas affecting the NMR active nuclei within a sample. PINES et al. discloses where markers, similar to a probe compound, such as lactate and citrate are studied to observe chemical processes on page 1, line 23. PINES et al. discloses where NMR spectroscopy can be used to observe the effects and changes of administered drugs on page 1, line 25.

Instant claim 5 requires the hyperpolarising step be carried out by one of means of polarization transfer from a noble gas, brute force, dynamic nuclear polarization (DNP), and spin refrigeration; PINES et al. teaches on pages 4-5 of

the Summary of Invention a method comprised of contacting a sample with a hyperpolarized noble gas.

Instant claim 6 requires the sample to be biofluids; PINES et al. discloses the use of the hyperpolarizing method with physiological fluids on pages 17-18 as well as defining these fluids on page 18, line 6.

Instant claim 25 requires the probe compounds to be substrates, inducers, or inhibitors of proteins selected from a group disclosed in the current instant claim. PINES et al. discloses the use of glycoproteins as samples on page 14, line 35; and discloses the use of proteins in the first paragraph of page 16.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 4, 24, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over W.O. 97/37239 A1 (PINES et al.) in view of U.S. Patent Application Publication 2003/0008924 A1 (WANG et al.).

Instant claim 4 requires the probe compounds are enriched with NMR active nuclei. Instant claim 24 and 26 require the probe compounds be enriched with at least one of ^{13}C and ^{15}N NMR active nuclei. PINES et al. discloses the use of NMR active nuclei such as ^{13}C and ^{15}N in the third paragraph of page 10. PINES et al. does not disclose the enriching of samples with these nuclei via labeling or synthesis as stated by the Specification of the instant application. However, WANG et al. discloses the labeling of protein samples for NMR studies in Paragraph [0246]. PINES et al. and WANG et al. are analogous art because they are in the same field of endeavor of studying biological compounds. At the time of the invention, it would have been obvious to one of ordinary skill in the art to enrich the samples of PINES et al. by using labeling technique of WANG et al. The motivation would have been for detecting the effects of the hyperpolarized gases on the sample to analyze the structure, chemistry, etc. of the sample (line 26 of page 10, PINES et al.) Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art the time the invention was made.

12. Claim 27 is rejected under 35 U.S.C. 103(a) as being obvious over W.O. 97/37239 A1 (PINES et al.).

Instant claim 27 requires that the probe compounds be selected from a group listed in the current instant claim; PINES et al. discloses on pages 14-16 descriptions of "samples" that can be analyzed using the method of hyperpolarizing claimed in the current application. Samples as defined by PINES et al. encompasses numerous material such as organic and inorganic monomers, inorganic and organic polymers, biopolymers, oligopeptides, polypeptides, antibodies, proteins, oligonucleotides, RNA polymers, DNA, chromosomes, genes, plasmids, carbohydrates, etc. PINES et al. does not explicitly state the compounds listed by instant claim 27. However, the description of "sample" meets the limitation of instant claim 27 by listing descriptions of compounds that can be analyzed as samples or combined with samples as probe compounds. Therefore, the invention as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. U.S. Patent 6,426,058 (PINES et al.) presents an invention that relates to methods that use hyperpolarized noble gases to enhance and improve NMR and MRI in *in vitro* and *in vivo* studies of biological systems in the Abstract.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRYAN T. KILPATRICK whose telephone number is (571)270-5553. The examiner can normally be reached on Mon - Fri (alt Fri off); 8:00 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Barbara Gilliam can be reached on 571-272-1330. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Barbara L. Gilliam/
Supervisory Patent Examiner, Art Unit 4128

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